

FIG._1

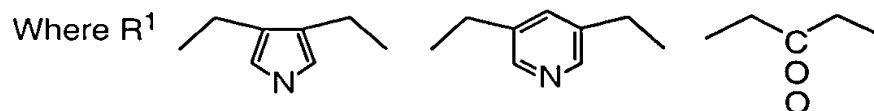
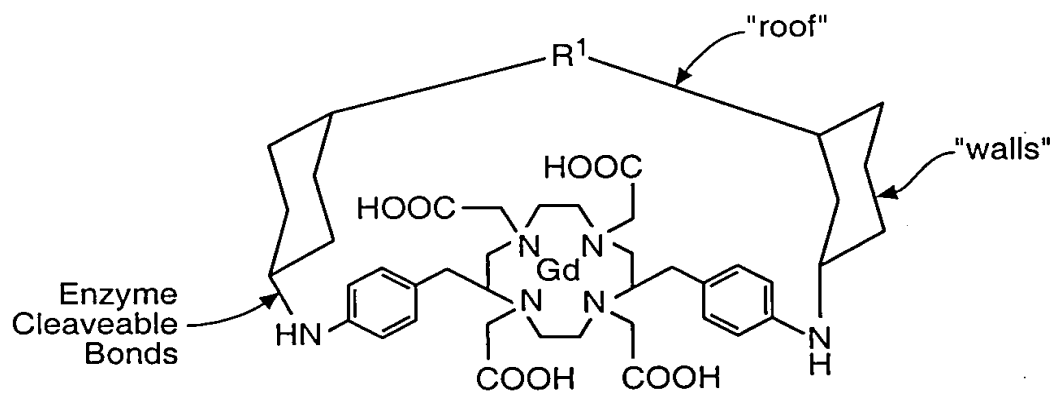


FIG._2

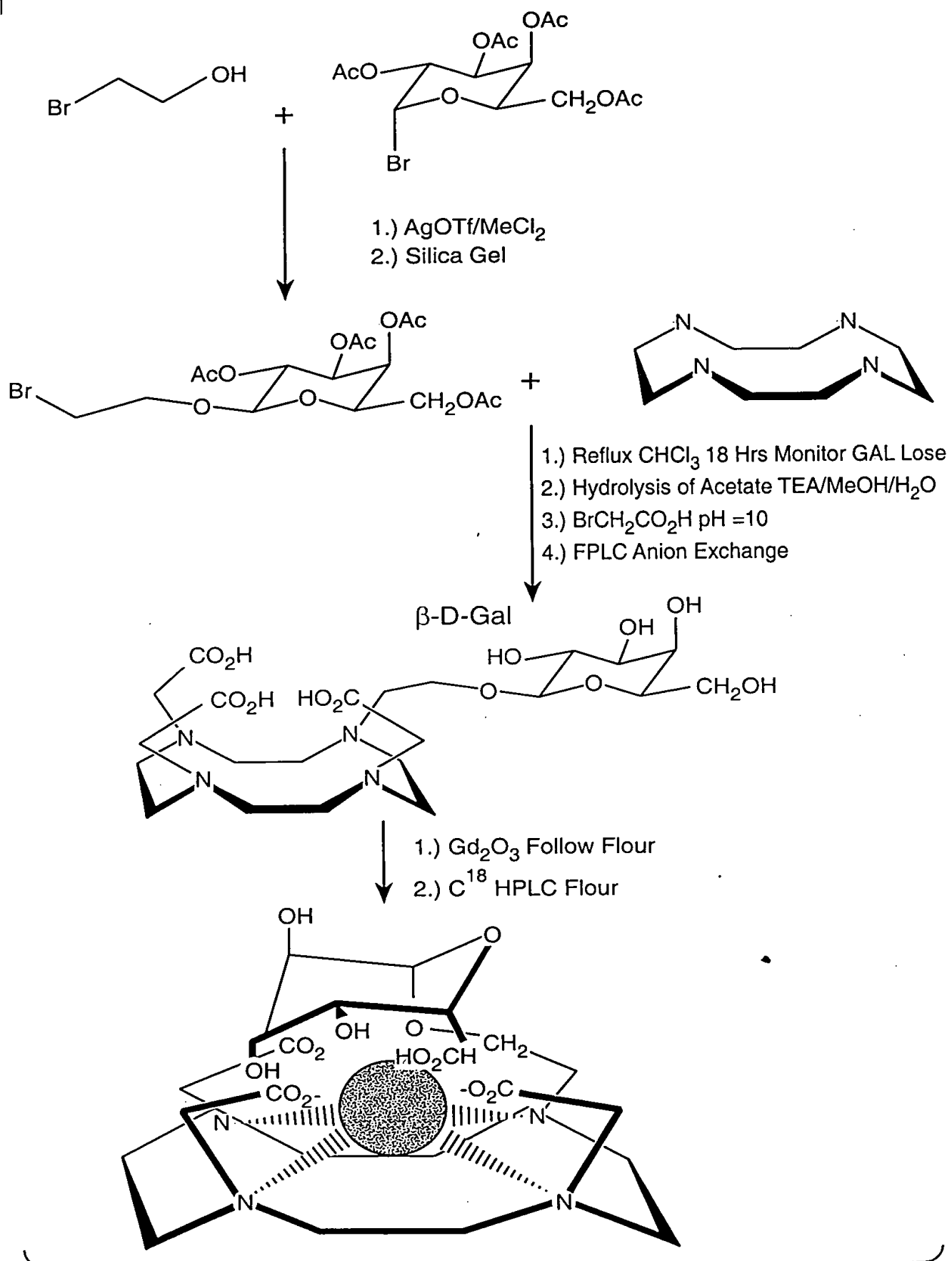
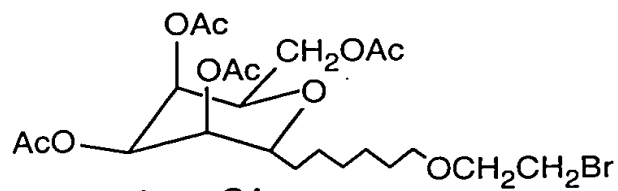


FIG. 3



2 = α OAc

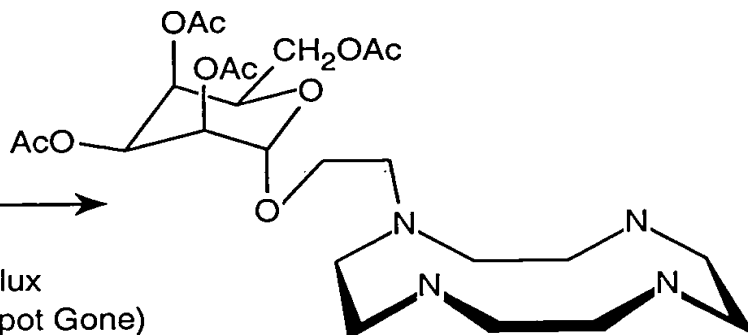
3 = β OAc

1 + 2

CHCl_3

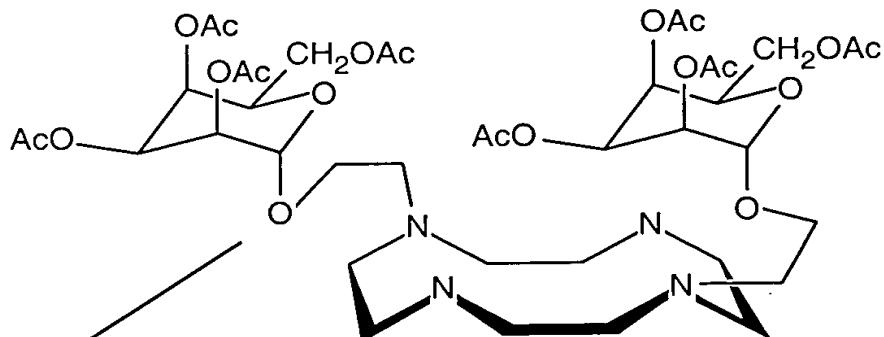
48 Hrs Reflux

T.L.C. (2 Spot Gone)



12 = α OH

(7 = β) 13 = β OH



(8 = β)

~2:1 6:5

Silica

4:1 $\text{CHCl}_3/\text{MeOH}$

8

1.) Hydrolysis Of Acetate
TCA/MeOH / H_2O

2.) $\text{BrCH}_2\text{CO}_2\text{H}$ pH = 10

3.) FPLC Cation Exchange
pH = 2 Acetic Acid Gradient

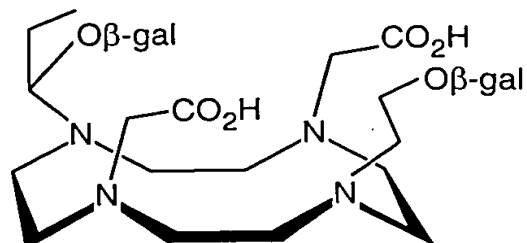


FIG. 4

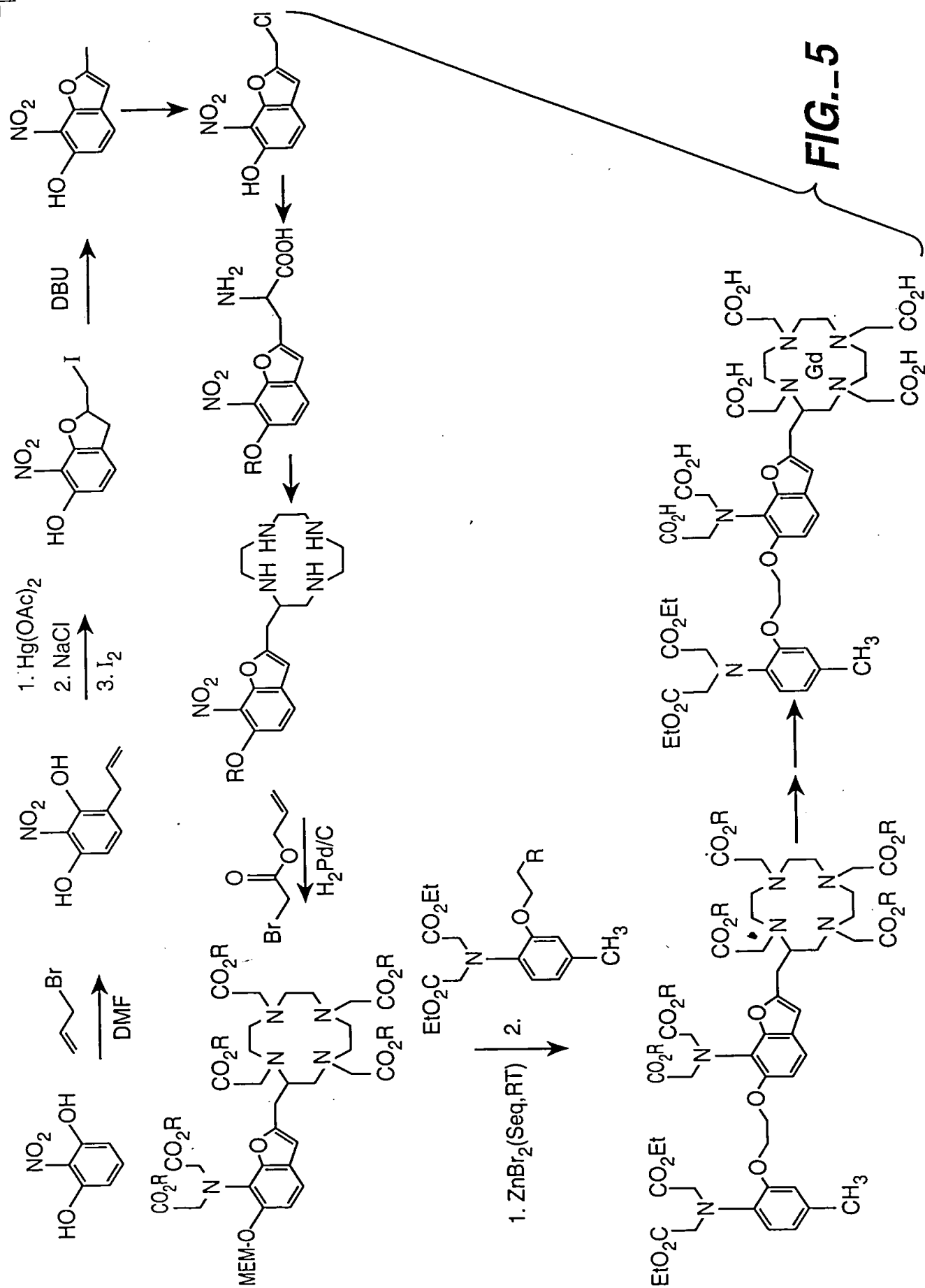


FIG. 5

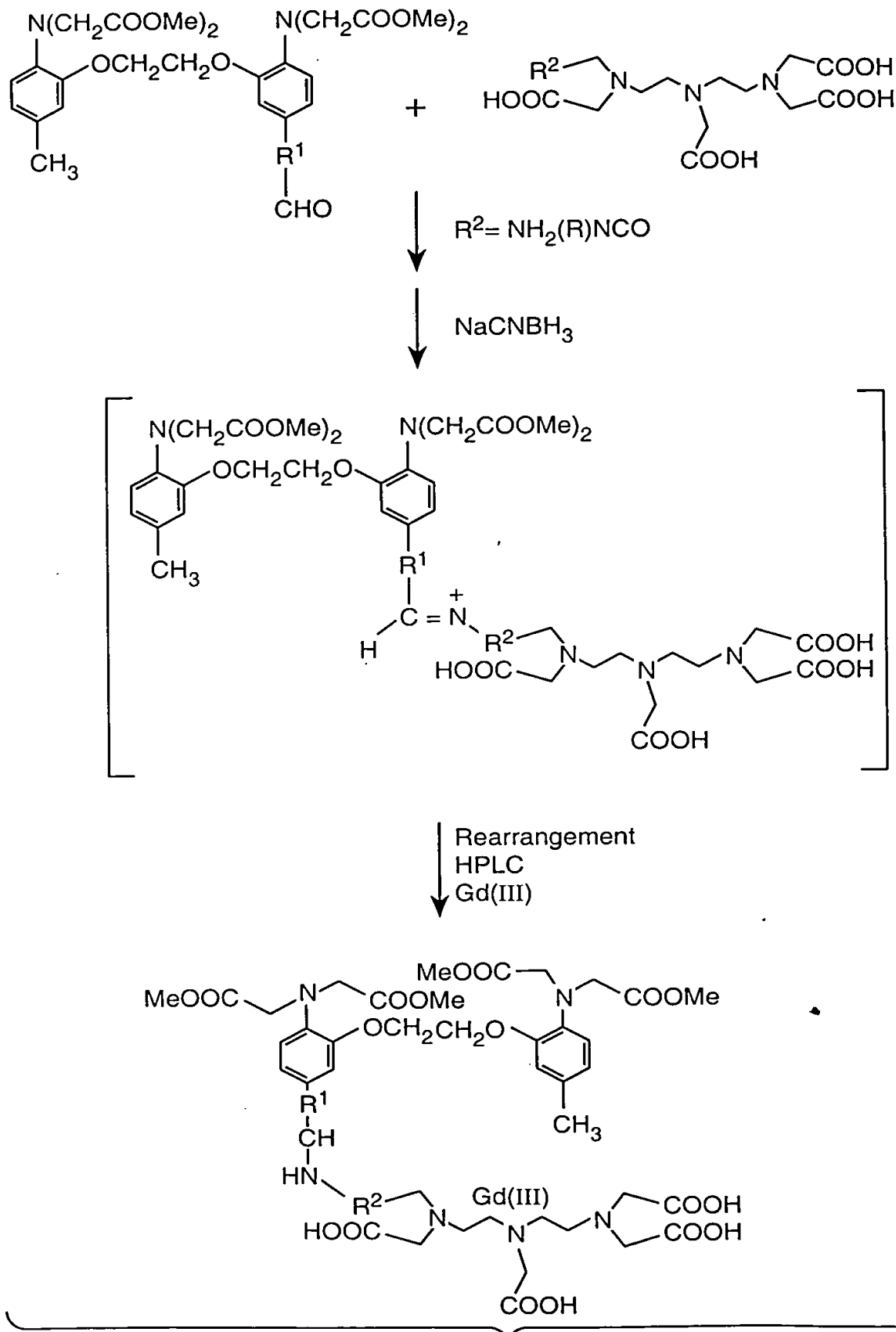
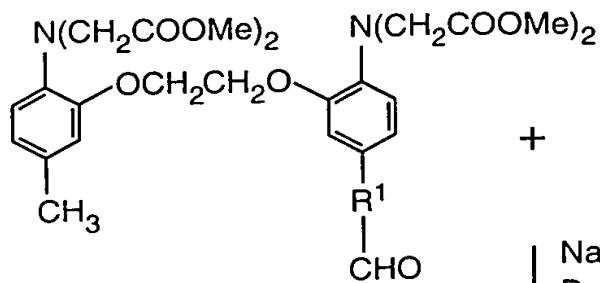
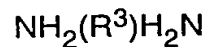


FIG. 7



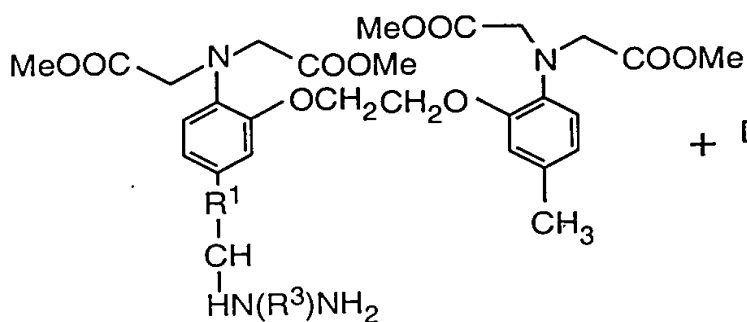
I.



+

\downarrow NaCNBH₃
 Dry MeOH
 Argon

HPLC



+ DTPA(Anhydride)

II.

HPLC

Gd(III)

Remove Protecting Groups

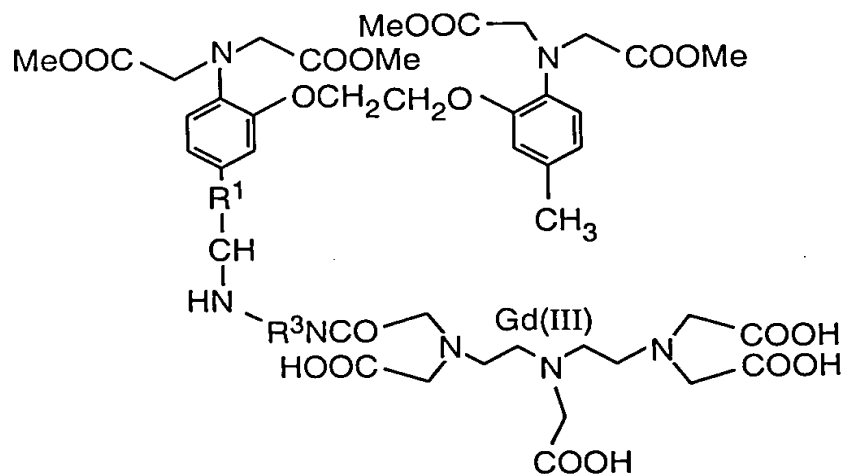


FIG. 8

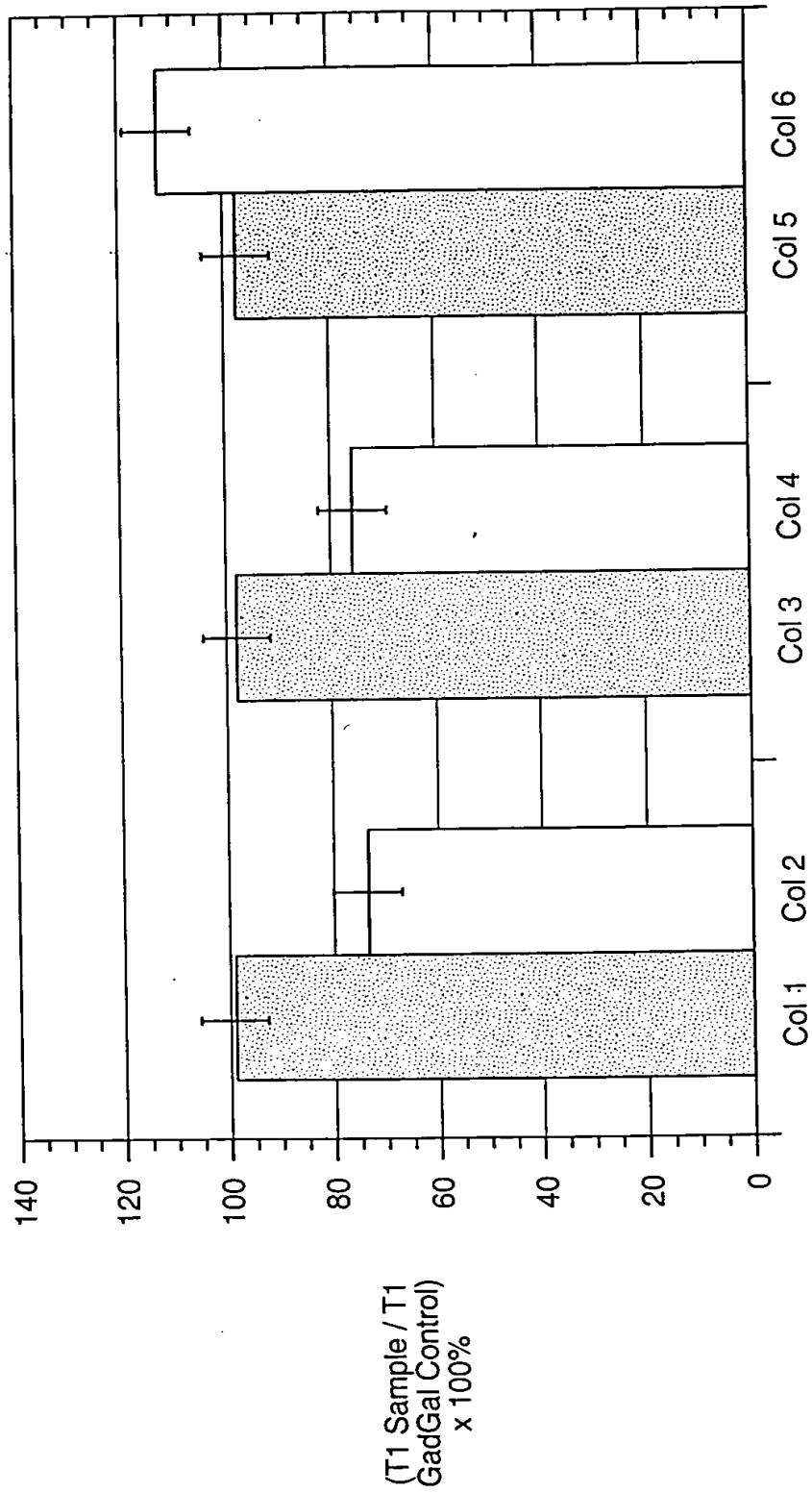


FIG.-9

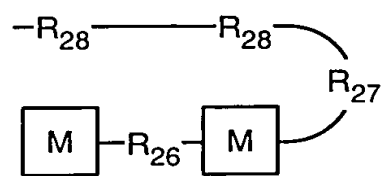


FIG. 10A

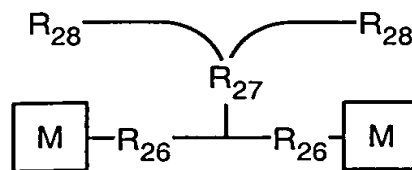


FIG. 10B

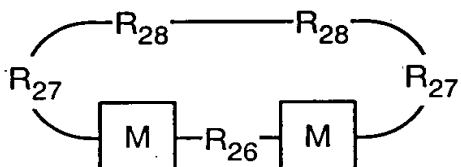


FIG. 10C

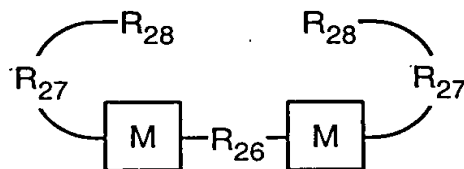


FIG. 10D

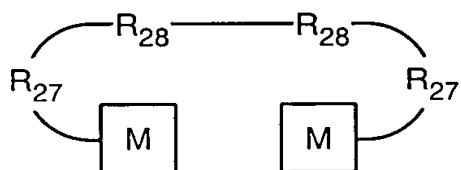


FIG. 10E

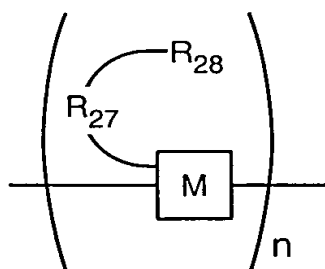


FIG. 10F

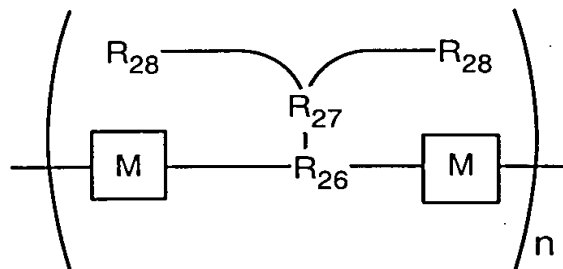


FIG. 10G

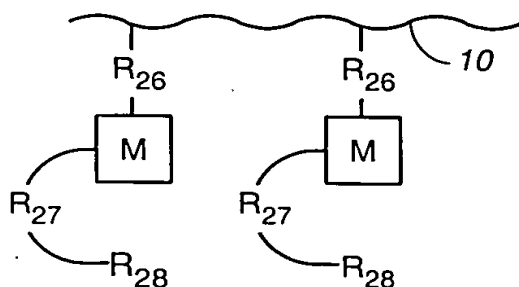


FIG. 10H

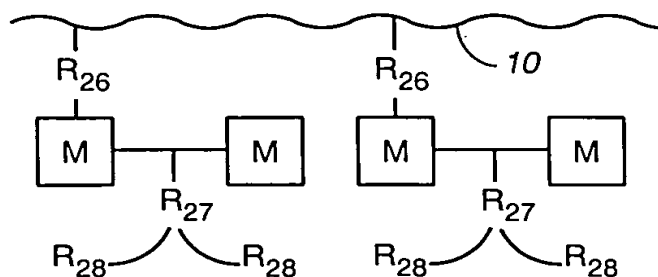
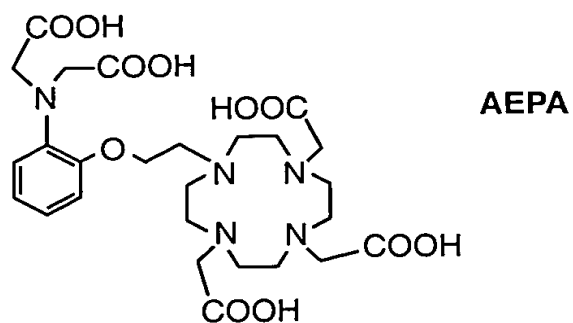


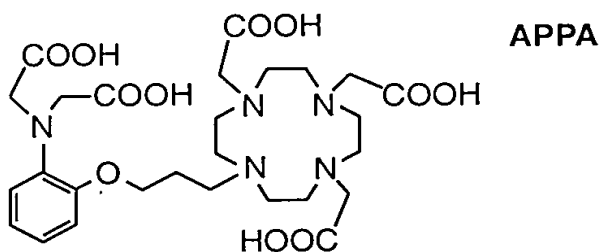
FIG. 10I

+



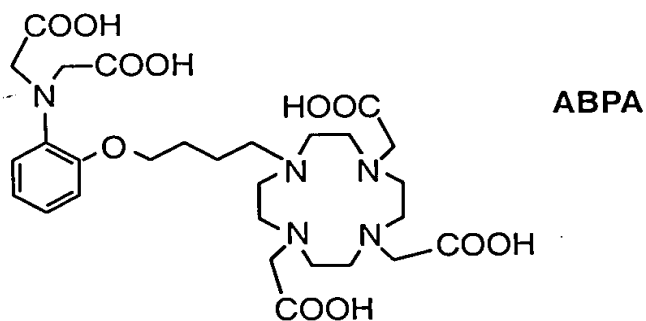
1-o-aminophenoxy-2-(cyclen)ethane-N,N,N',N'',N'''-pentaacetic acid

FIG._ 11A



1-o-aminophenoxy-3-(cyclen)propane-N,N,N',N'',N'''-pentaacetic acid

FIG._ 11B



1-o-aminophenoxy-4-(cyclen)butane-N,N,N',N'',N'''-pentaacetic acid

FIG._ 11C

09866513_052401
T04250"27599860

+

+

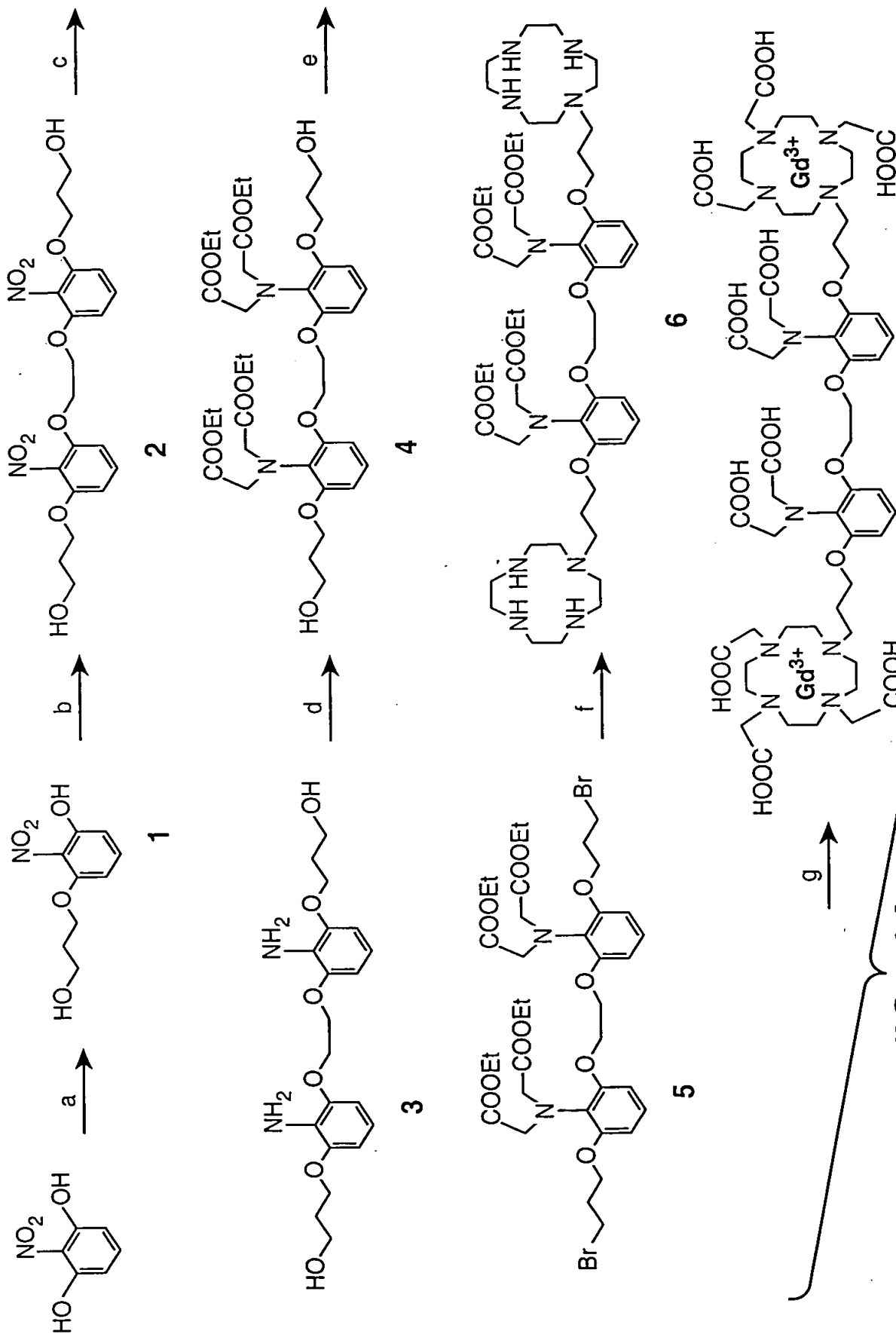


FIG. 14

+

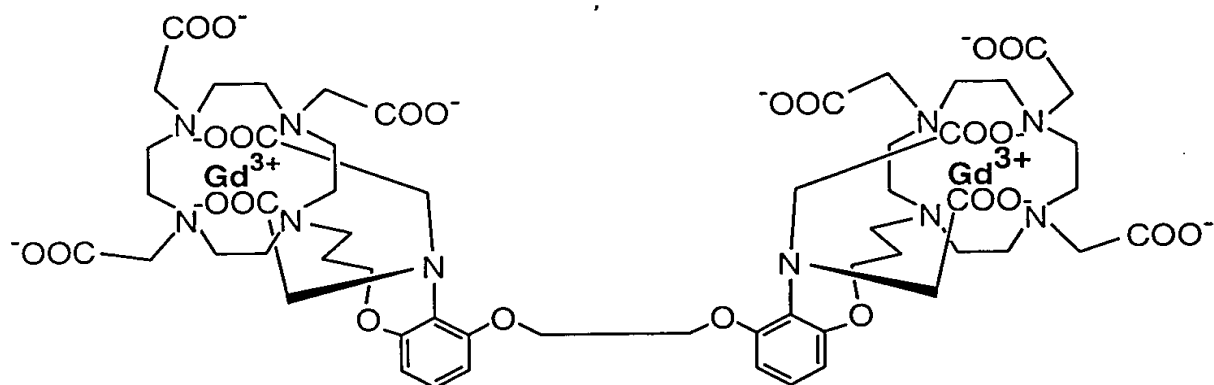
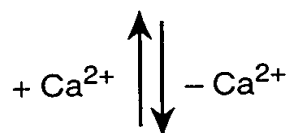
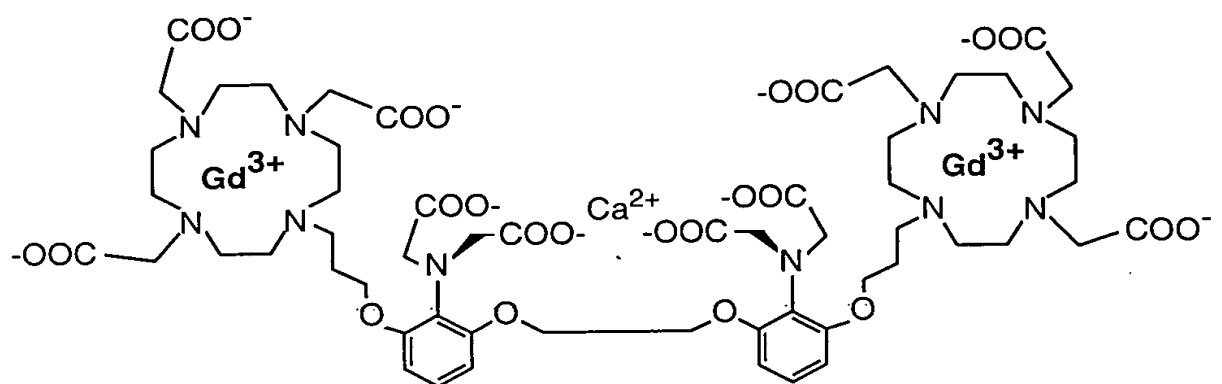


FIG. 15

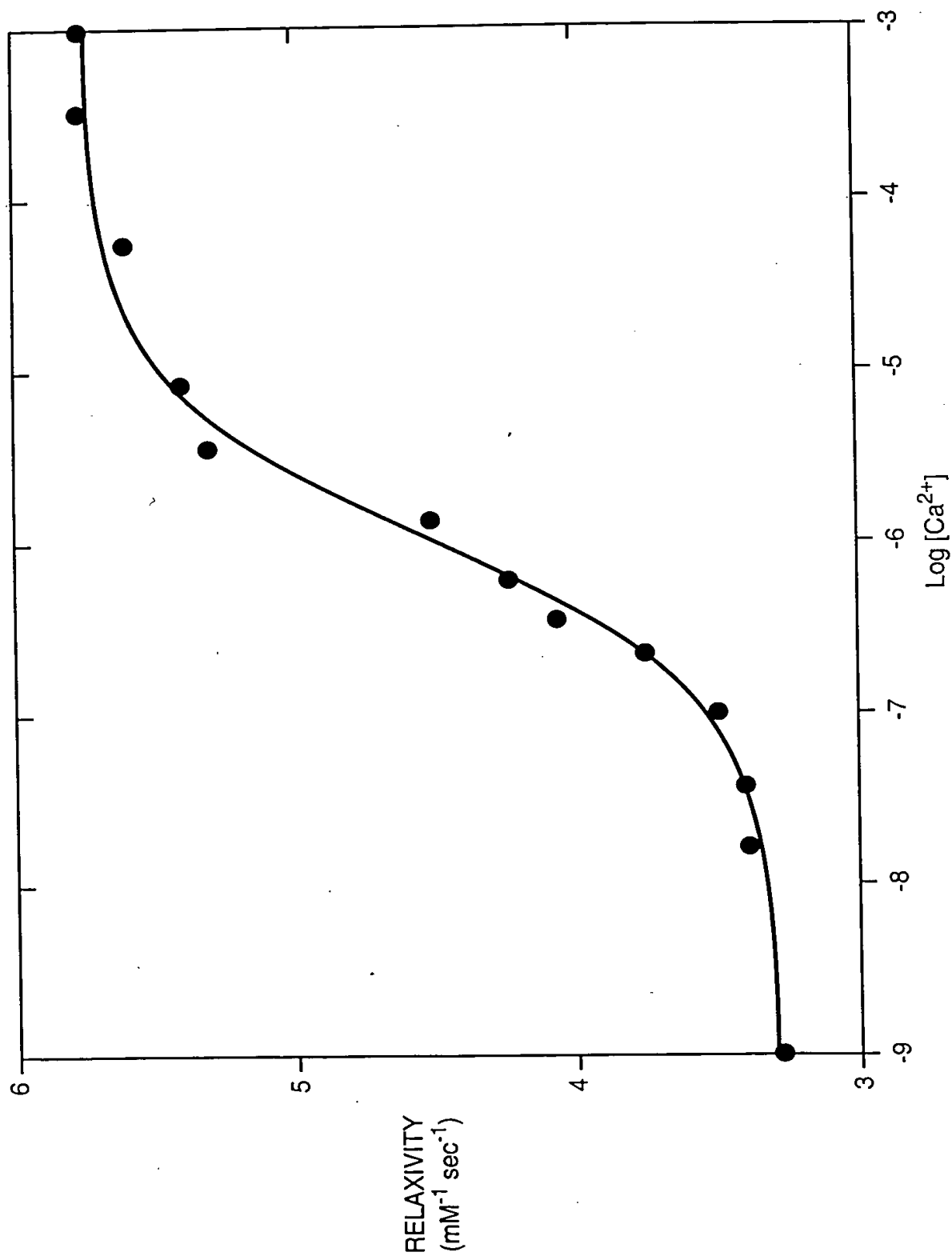


FIG. 16

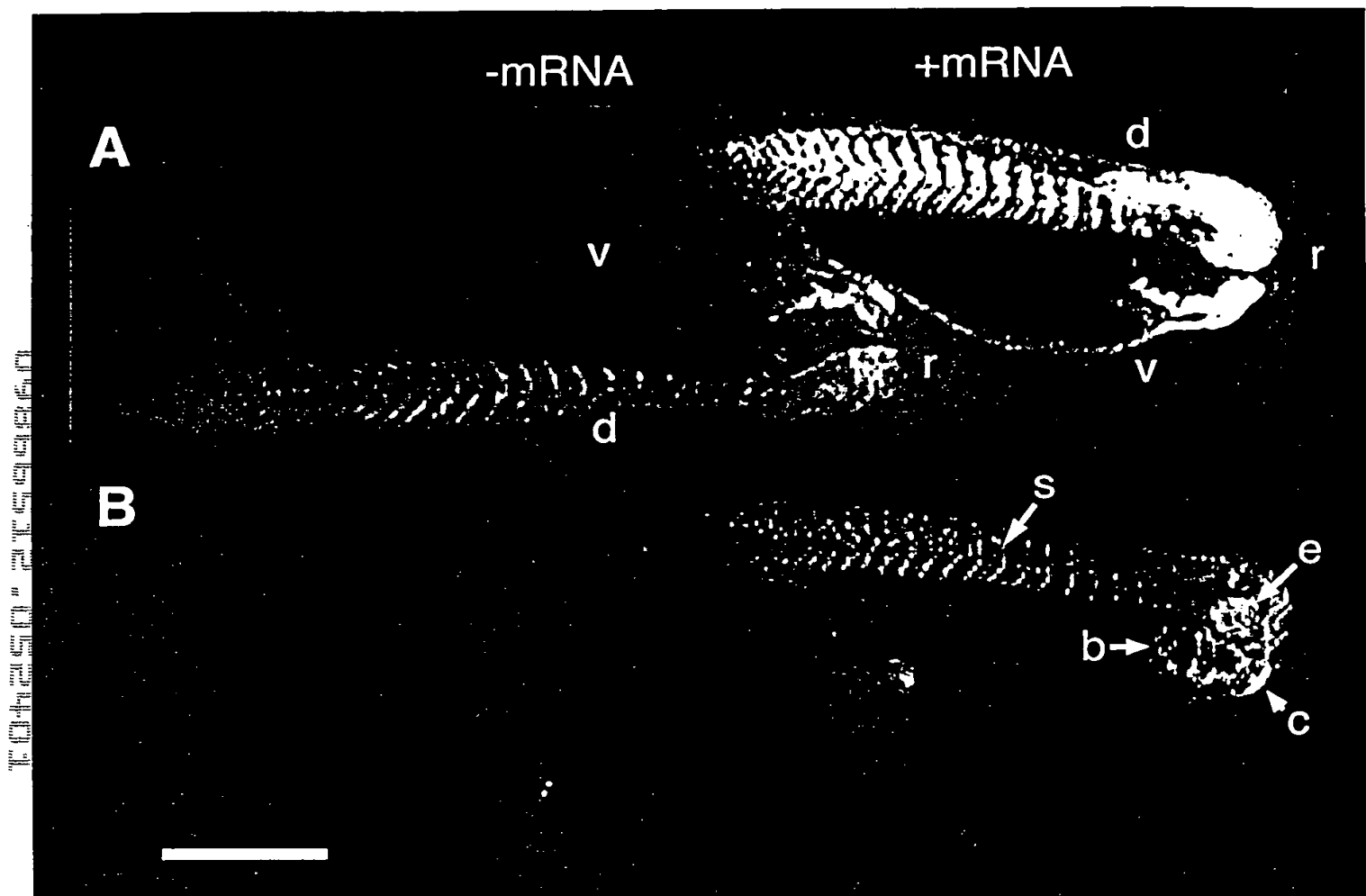


FIG._17

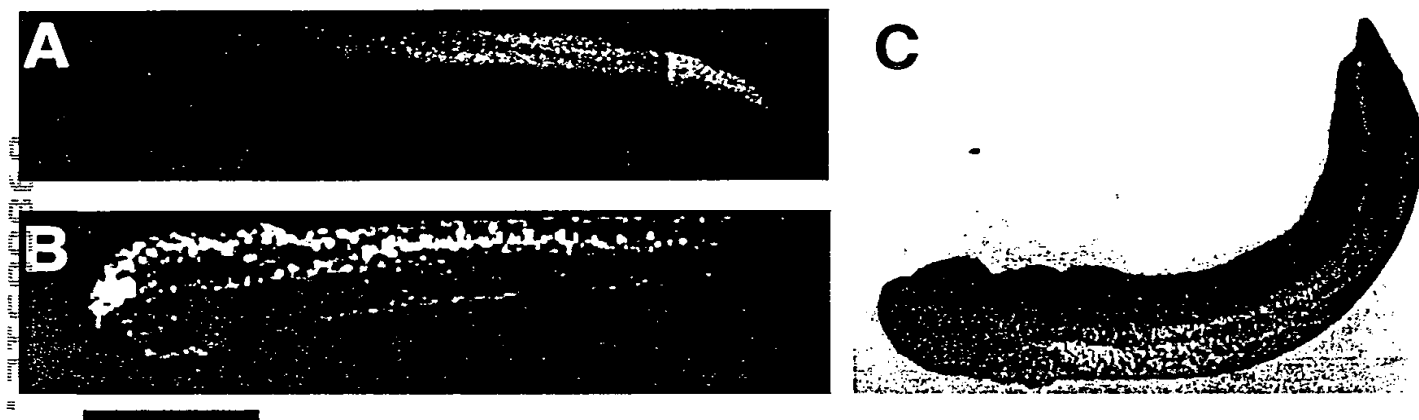


FIG._18

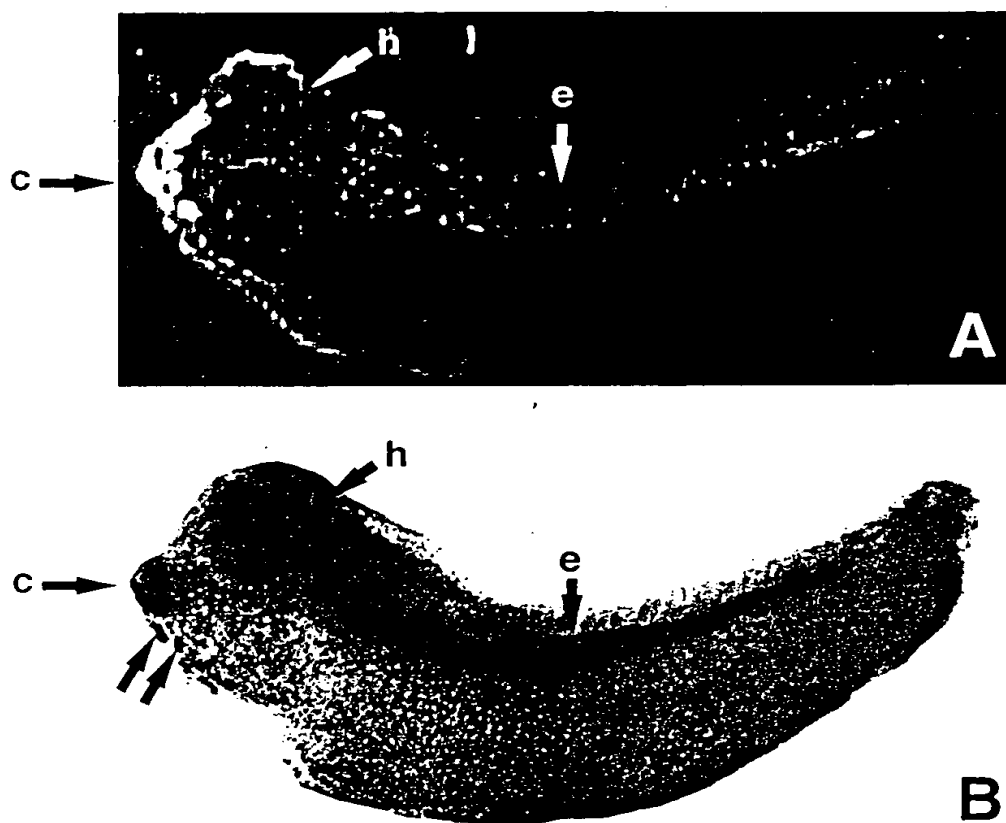


FIG._19

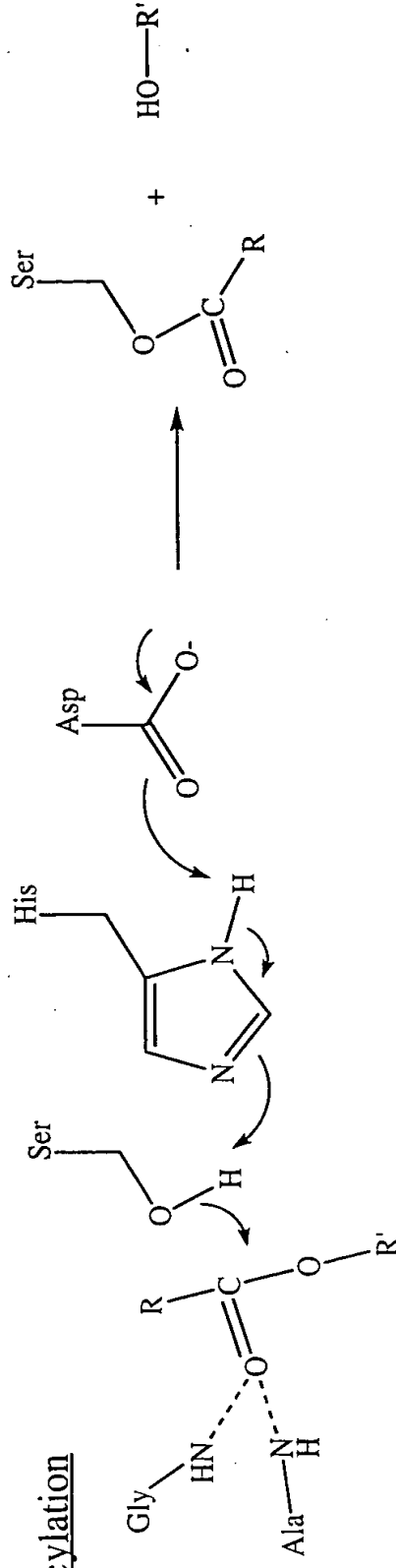
Properties of Carboxylesterases:

1. Efficient cleavage of Ester functional groups

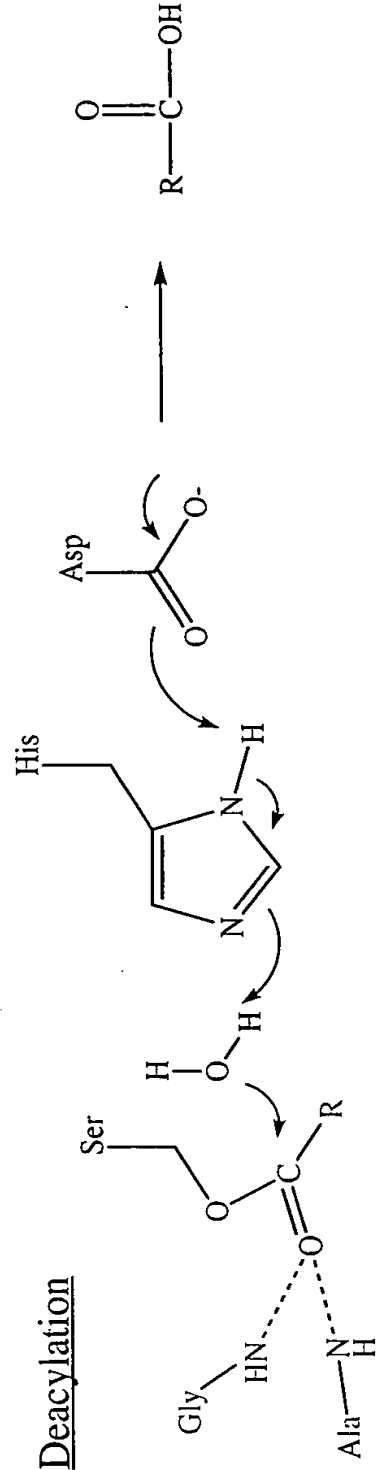


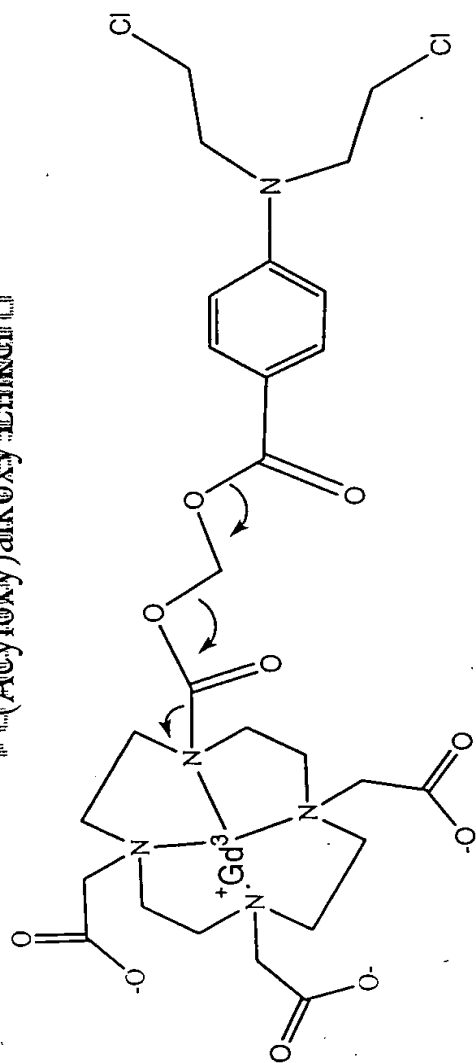
2. Belongs to the family of Ser-His-Asp active site enzymes (serine protease)

Acylation

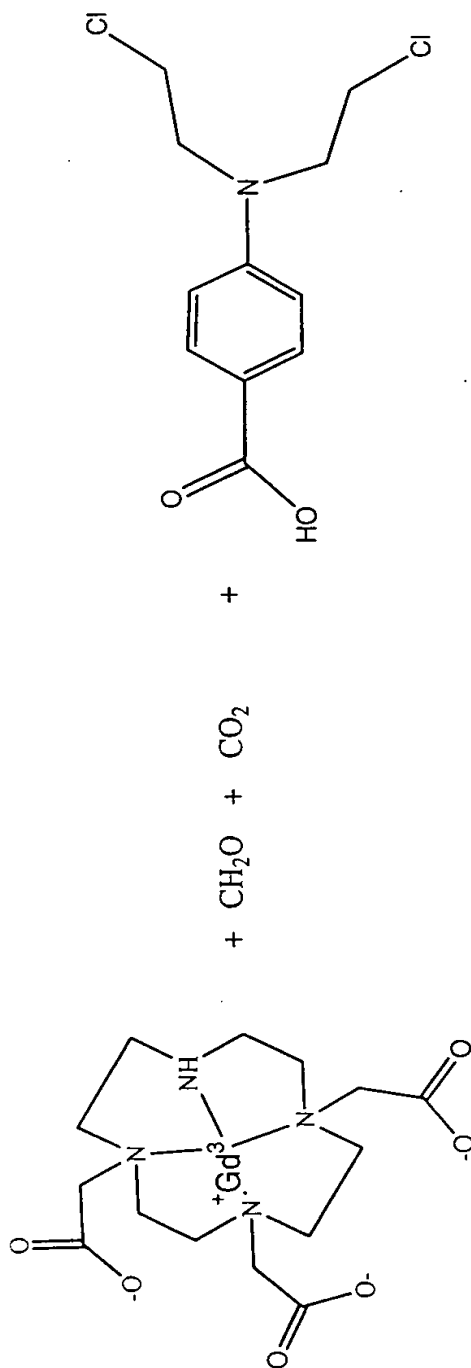


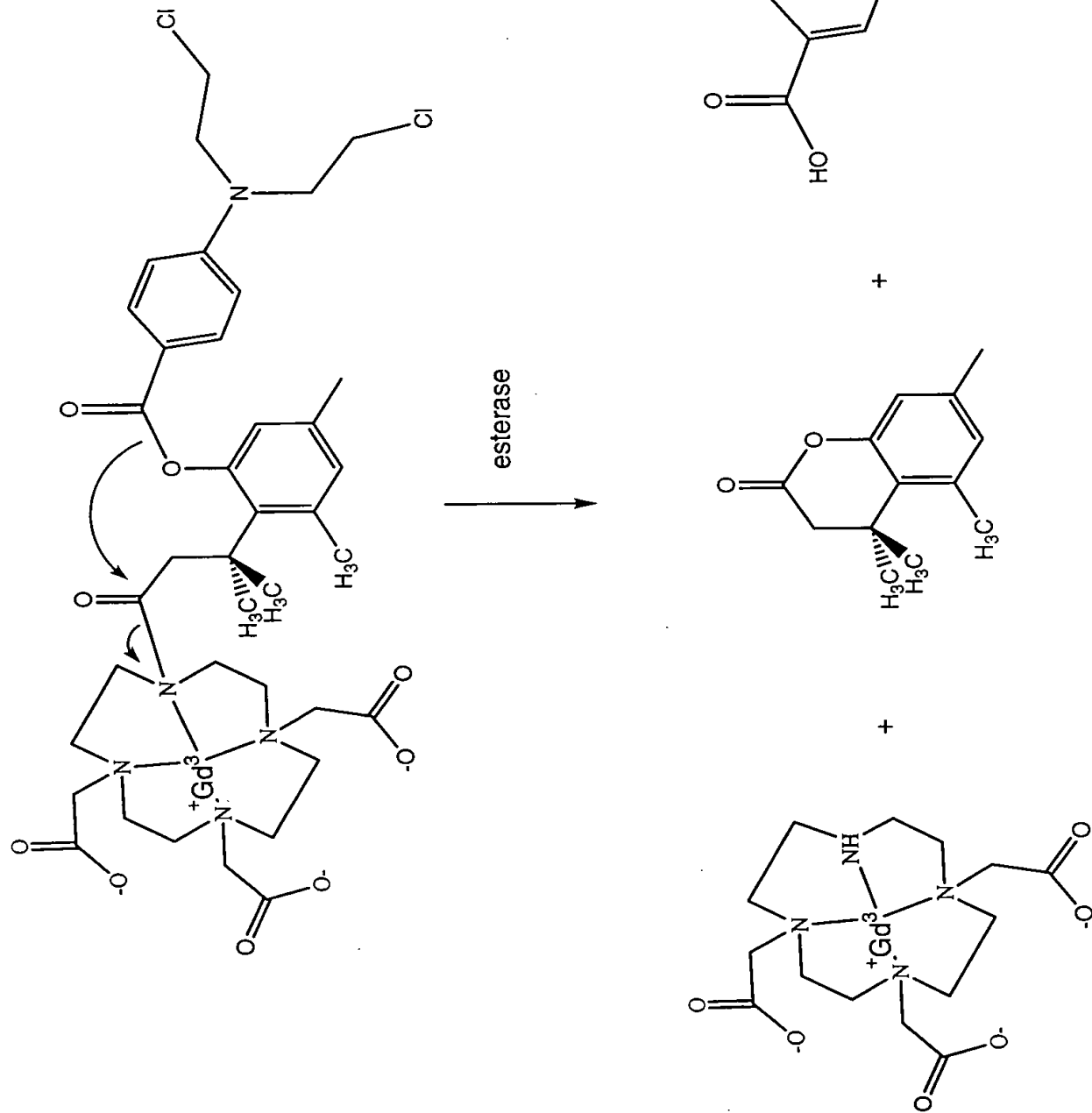
Deacylation





esterase





Fmoc Chemistry for Synthesis of Linker Peptide unit

I.

MBHA Rink Amide Resin

or

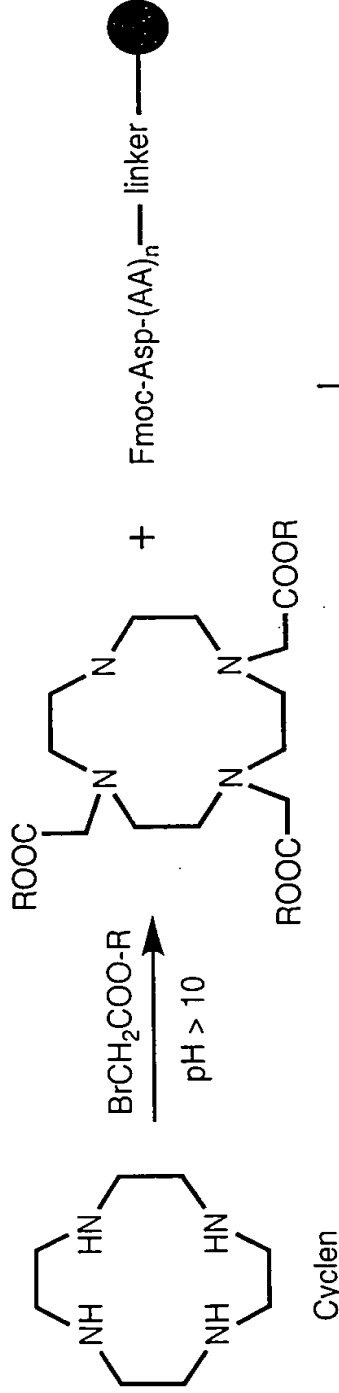
PAL-PEG-PS Resin

Activation with 20% piperidine
in DMF

Fmoc AA-OH/HOAt/HATU/DIEA

1. N-ε-Fmoc-ε-amino-R acid
[H₂C(CH₂)_x-NH-Fmoc]
2. Fmoc-AA-OH
3. Fmoc-AA-OH
4. (Fmoc-AA-OH)_n
5. Fmoc-Asp-OH

II.



III.

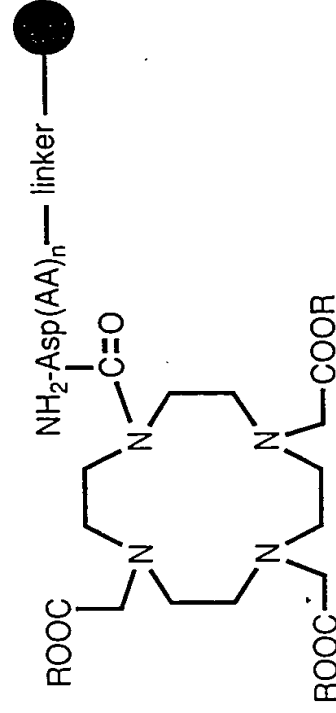
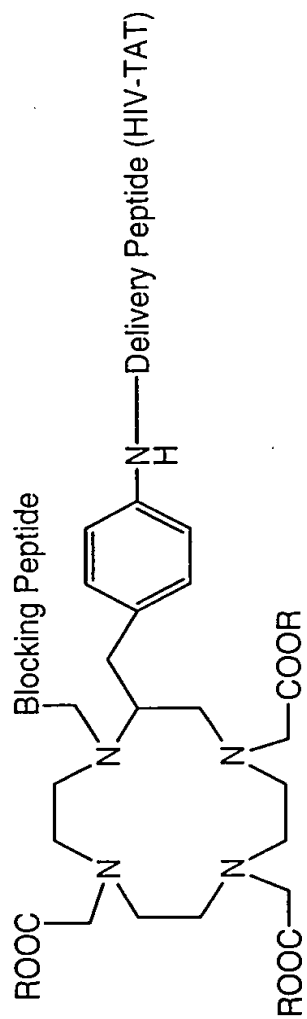


Fig 21



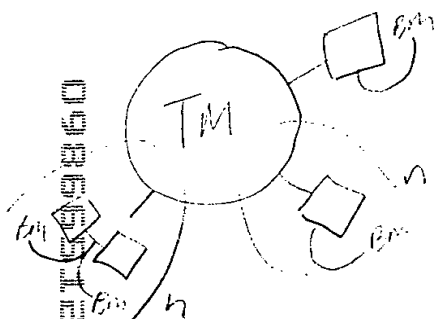
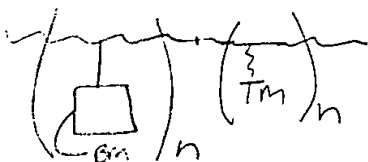
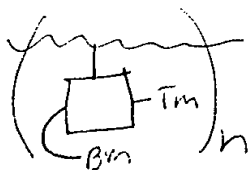
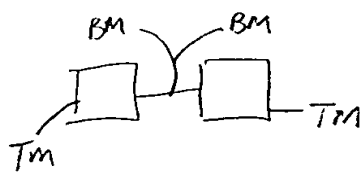
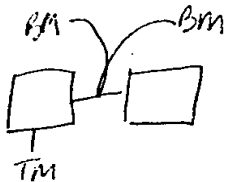
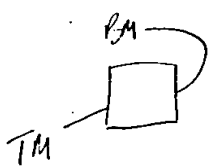


FIG 23